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more stable and exhibited better long-term storage stability, with significantly less degradation (% Total Deg. Products) than the monofumarate form. Conditions evaluated include temperature, relative humidity (RH), and the open or closed state of the container cap.

TABLE 3

Chemical Stability Comparison					
		Monofumarate form		Hemifumarate form	
Storage Condition	Time Points (weeks)	% TA * Area Normalized	% Total Deg. Products	% TA Area Normalized	% Total Deg. Products
40° C./	0	97.1	0.69	98.4	0.05
75% RH	1	97.0	0.87	98.4	0.14
Cap	2	96.6	1.18	98.5	0.14
Closed	4	96.4	1.49	98.4	0.25
	8	95.4	2.36	98.0	0.49
40° C./	0	97.1	0.69	98.4	0.05
75% RH	1	96.9	0.90	98.5	0.15
Сар	2	96.6	1.10	98.5	0.14
Open	4	96.2	1.67	98.4	0.26
•	8	95.0	2.74	98.1	0.50
70° C.	0	97.1	0.69	98.4	0.05
Сар	2	96.2	1.83	98.5	0.22
Closed	4	93.3	4.78	98.4	0.33

<sup>\*</sup> TA is tenofovir alafenamide

## Thermodynamic Stability

Stable form screening of tenofovir alafenamide hemifumarate showed that it is thermodynamically stable in most solvents, such as ACN, toluene, ethyl acetate, methyl tert-butyl ether (MTBE), acetone, THF, and 2-methyl THF. A similar stable form screening of the monofumarate form showed that this form is not thermodynamically stable in the above-listed solvents. When suspended in these solvents, the monofuma- 35 rate form of tenofovir alafenamide fully converts to the hemifumarate form in THF and 2-methyl THF, and partially converts to the hemifumarate form in ACN, ethyl acetate, MTBE, and acetone, as well as at ambient temperatures.

## Thermal Stability

As shown by the DSC data, the hemifumarate form of tenofovir alafenamide has a melting point that is about 10° C. higher than that of the monofumarate form, indicating that the hemifumarate form has improved thermal stability as compared with the monofumarate form.

All publications, patents, and patent documents are incorporated by reference herein, as though individually incorporated by reference. The invention has been described with reference to various specific and preferred embodiments and techniques. However, it should be understood that many 50 variations and modifications may be made while remaining within the spirit and scope of the invention.

What is claimed is:

- 1. Tenofovir alafenamide hemifumarate.
- scanning calorimetry (DSC) onset endotherm of 131±2° C.
- 3. The hemifumarate of claim 2 that has a DSC onset endotherm of 131±1° C.
- 4. Tenofovir alafenamide hemifumarate, having an X-ray powder diffraction (XRPD) pattern comprises 2theta values 60 of 6.9±0.2° and 8.6±0.2°.
- 5. The hemifumarate of claim 4, wherein the XRPD pattern comprises 2theta values of  $6.9\pm0.2^{\circ}$ ,  $8.6\pm0.2^{\circ}$ ,  $11.0\pm0.2^{\circ}$ , 15.9±0.2°, and 20.2±0.2°.
- 6. A composition comprising tenofovir alafenamide hemi- 65 fumarate according to claim 1, wherein the ratio of fumaric acid to tenofovir alafenamide in said composition is 0.5±0.1.

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- 7. The composition of claim 6, wherein the ratio of fumaric acid to tenofovir alafenamide is 0.5±0.05.
- 8. The composition of claim 6, wherein the ratio of fumaric acid to tenofovir alafenamide is  $0.5\pm0.01$ .
- 9. The composition of claim 6, wherein the ratio of fumaric acid to tenofovir alafenamide is about 0.5.
  - 10. The composition of claim 6, which is a solid.
- 11. A pharmaceutical composition comprising the hemifumarate of claim 1 and a pharmaceutically acceptable excipi-
- 12. The pharmaceutical composition of claim 11, further comprising an additional therapeutic agent.
- 13. The pharmaceutical composition of claim 12, wherein 15 the additional therapeutic agent is selected from the group consisting of human immunodeficiency virus (HIV) protease inhibiting compounds, HIV nonnucleoside inhibitors of reverse transcriptase, HIV nucleoside inhibitors of reverse transcriptase, HIV nucleotide inhibitors of reverse transcriptase, HIV integrase inhibitors, and CCR5 inhibitors.
  - 14. The composition of claim 7, which is a solid.
  - 15. The composition of claim 8, which is a solid.
  - 16. The composition of claim 9, which is a solid.
  - 17. A method for treating a human immunodeficiency virus (HIV) infection comprising administering to a subject in need thereof a therapeutically effective amount of the hemifumarate of claim 1.
  - 18. A method for treating an HIV infection comprising administering to a subject in need thereof a therapeutically effective amount of the pharmaceutical composition of claim 11.
  - 19. The method for treating an HIV infection of claim 17, further comprising administering to the subject one or more additional therapeutic agents selected from the group consisting of HIV protease inhibiting compounds, HIV nonnucleoside inhibitors of reverse transcriptase, HIV nucleoside inhibitors of reverse transcriptase, HIV nucleotide inhibitors of reverse transcriptase, HIV integrase inhibitors, and CCR5 inhibitors.
  - 20. A method for treating a hepatitis B virus (HBV) infection comprising administering to a subject in need thereof a therapeutically effective amount of the hemifumarate of claim 1.
  - 21. A method for treating an HBV infection comprising administering to a subject in need thereof a therapeutically effective amount of the pharmaceutical composition of claim
  - 22. The method for treating an HIV infection of claim 17, wherein the hemifumarate is administered in multiple daily doses.
  - 23. The method for treating an HIV infection of claim 17, wherein the hemifumarate is administered in a single daily
- 24. The method for treating an HBV infection of claim 20, 2. The hemifumarate of claim 1 that has a differential 55 wherein the hemifumarate is administered in multiple daily
  - 25. The method for treating an HBV infection of claim 20, wherein the hemifumarate is administered in a single daily
  - 26. A method for preparing a pharmaceutical composition comprising combining the hemifumarate of claim 1 and a pharmaceutically acceptable excipient to provide the pharmaceutical composition.
  - 27. A method for preparing tenofovir alafenamide hemifumarate comprising admixing a) aprotic organic solvent; b) fumaric acid; c) tenofovir alafenamide; and d) one or more seeds of tenofovir alafenamide hemifumarate; and